Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Phase-III Study of Adjuvant Regorafenib Versus Placebo for Patients with Stage IV Colorectal Cancer After Curative Treatment of Liver Metastases

Summary

EudraCT number	2012-004369-42
Trial protocol	BE ES GB IT DE FR
Global end of trial date	29 August 2016

Results information

Result version number	v1 (current)
This version publication date	18 August 2017
First version publication date	18 August 2017

Trial information

Trial identification

Sponsor protocol code	BAY73-4506/15983

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01939223
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee , Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 August 2016
Global end of trial reached?	Yes
Global end of trial date	29 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate and compare the efficacy and safety of regorafenib versus placebo in subjects with colorectal cancer (CRC) after curative resection of liver metastasis and completion of all planned chemotherapy.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	China: 1
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	25
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	18
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multinational study was conducted at 32 study centers that screened 65 subjects across 9 countries, between 02 December 2013 (start of enrollment) and 29 August 2016 (last patient last vist).

Pre-assignment

Screening details:

Overall, 65 subjects were screened, of which 40 were screen failures. The remaining 25 subjects were randomized and assigned to treatment. All 25 subjects received treatment.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Regorafenib 160 mg

Arm description:

Description: Subjects received regorafenib 160 milligram (mg) (4 * 40 mg tablets) orally once daily on a 3 weeks on / 1 week off dosing schedule.

Arm type	Experimental
Investigational medicinal product name	Regorafenib
Investigational medicinal product code	BAY73-4506
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received regorafenib 160 milligram (mg) (4 * 40 mg tablets) orally once daily on a 3 weeks on / 1 week off dosing schedule.

Arm title	Placebo

Arm description:

Subjects received placebo matching to regorafenib tablet orally once daily on a 3 weeks on / 1 week off dosing schedule.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching to regorafenib tablet orally once daily on a 3 weeks on / 1 week off dosing schedule.

Number of subjects in period 1	Regorafenib 160 mg	Placebo
Started	14	11
Participants received treatment	14	11
Completed	1	0
Not completed	13	11
AE not associated with disease recurrence	1	1
Consent withdrawn by subject	6	-
Disease recurrence (radiological recurrence)	1	3
Study stopped by Sponsor	5	7

Baseline characteristics

Reporting groups	
Reporting group title	Regorafenib 160 mg
Reporting group description:	
Description: Subjects received regorafenib 160 milligram (mg) (4 * 40 mg tablets) orally once daily on a 3 weeks on / 1 week off dosing schedule.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matching to regorafenib tablet orally once daily on a 3 weeks on / 1 week off dosing schedule.	

Reporting group values	Regorafenib 160 mg	Placebo	Total
Number of subjects	14	11	25
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59.7	57	
standard deviation	± 11.22	± 9.83	-
Gender categorical Units: Subjects			
Female	9	5	14
Male	5	6	11

End points

End points reporting groups

Reporting group title	Regorafenib 160 mg

Reporting group description:

Description: Subjects received regorafenib 160 milligram (mg) (4 * 40 mg tablets) orally once daily on a 3 weeks on / 1 week off dosing schedule.

Reporting group title	Placebo

Reporting group description:

Subjects received placebo matching to regorafenib tablet orally once daily on a 3 weeks on / 1 week off dosing schedule.

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set (FAS) (N = 25): all subjects who were assigned to treatment.

Primary: Disease Free Survival (DFS) as assessed by the investigator

End point title	Disease Free Survival (DFS) as assessed by the investigator[1]

End point description:

Disease free survival was evaluated by CT / MRI scans as assessed by the investigator, which was defined as the time (in days) from date of randomization to date of first observed radiographic disease recurrence (RECIST 1.1 criteria for measurable and non-measurable disease) or death due to any cause, if death occurred before disease recurrence was documented. For subjects without documented disease recurrence or death at the time of analysis, the DFS time was censored at the date of the last evaluable CT / MRI scan.

End point type	Primary

End point timeframe:

From date of randomization to date of first observed radiographic disease recurrence (RECIST 1.1 criteria for measurable and non-measurable disease) or death due to any cause, if death occurred before disease recurrence was documented.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was prematurely terminated. Analysis was not performed for this endpoint.

End point values	Regorafenib 160 mg	Placebo	Full analysis set (FAS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: days				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[2] - This study was prematurely terminated. Analysis was not performed for this endpoint.

[3] - This study was prematurely terminated. Analysis was not perfomed for this endpoint.

[4] - This study was prematurely terminated. Analysis was not perfomed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival (OS) is defined as the time (days) from randomization to death due to any cause. The

OS time for subjects alive at the time of analysis will be censored at their last date known to be alive.

End point type	Secondary

End point timeframe:

Subjects who experienced disease recurrence (either during treatment or during Active Follow-up), or otherwise withdrew from the study for any reason other than death, were followed for overall survival unless consent was withdrawn.

End point values	Regorafenib 160 mg	Placebo	Full analysis set (FAS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: days				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[5] - This study was prematurely terminated. Analysis was not perfomed for this endpoint.

[6] - This study was prematurely terminated. Analysis was not perfomed for this endpoint.

[7] - This study was prematurely terminated. Analysis was not perfomed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study treatment until 30 days after the last study drug intake	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Regorafenib 160 mg (BAY73-4506)
Reporting group description:	
Subjects received regorafenib 160 mg (4 *40 mg tablets) orally every day for 3 weeks followed by 1 week off treatment plus BSC (best supportive care).	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to regorafenib tablets orally every day for 3 weeks followed by 1 week off treatment plus BSC (best supportive care).	

Serious adverse events	Regorafenib 160 mg (BAY73-4506)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Regorafenib 160 mg (BAY73-4506)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	10 / 11 (90.91%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hair follicle tumour benign			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 14 (50.00%)	1 / 11 (9.09%)	
occurrences (all)	29	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 14 (28.57%)	2 / 11 (18.18%)	
occurrences (all)	6	2	
Chills			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	2 / 14 (14.29%)	3 / 11 (27.27%)	
occurrences (all)	2	3	
Mucosal inflammation			
subjects affected / exposed	0 / 14 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Non-cardiac chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	3 / 14 (21.43%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Immune system disorders			
Contrast media allergy			

subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	5 / 14 (35.71%)	1 / 11 (9.09%)	
occurrences (all)	5	1	
Nasal congestion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Rhinitis atrophic			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 14 (14.29%)	1 / 11 (9.09%)	
occurrences (all)	6	2	
Amylase increased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 14 (28.57%)	0 / 11 (0.00%)	
occurrences (all)	10	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Blood bilirubin increased			

subjects affected / exposed	5 / 14 (35.71%)	0 / 11 (0.00%)		
occurrences (all)	7	0		
Blood bilirubin unconjugated increased				
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)		
occurrences (all)	2	0		
Blood creatinine decreased				
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)		
occurrences (all)	0	1		
Blood lactate dehydrogenase increased				
subjects affected / exposed	3 / 14 (21.43%)	0 / 11 (0.00%)		
occurrences (all)	3	0		
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)		
occurrences (all)	2	1		
Lipase increased				
subjects affected / exposed	4 / 14 (28.57%)	1 / 11 (9.09%)		
occurrences (all)	7	4		
Lymphocyte count decreased				
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)		
occurrences (all)	2	0		
Neutrophil count decreased				
subjects affected / exposed	2 / 14 (14.29%)	0 / 11 (0.00%)		
occurrences (all)	3	0		
Neutrophil count increased				
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)		
occurrences (all)	1	0		
Platelet count decreased				
subjects affected / exposed	4 / 14 (28.57%)	0 / 11 (0.00%)		
occurrences (all)	9	0		
Weight decreased				
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)		
occurrences (all)	1	0		
Weight increased				

subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
White blood cell count decreased			
subjects affected / exposed	3 / 14 (21.43%)	0 / 11 (0.00%)	
occurrences (all)	5	0	
White blood cell count increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
White blood cells urine positive			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Thermal burn			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Neuropathy peripheral			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 14 (14.29%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Febrile neutropenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Anal fistula			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Cheilitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	4 / 14 (28.57%)	2 / 11 (18.18%)	
occurrences (all)	5	2	
Dental caries			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	3 / 11 (27.27%)	
occurrences (all)	1	5	
Flatulence			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Gingival pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nausea			

subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	1	2	
Stomatitis			
subjects affected / exposed	2 / 14 (14.29%)	2 / 11 (18.18%)	
occurrences (all)	2	2	
Toothache			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Dermatitis acneiform			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Dermatitis bullous			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Erythema multiforme			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Generalised erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Hyperkeratosis			

subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	6 / 14 (42.86%)	1 / 11 (9.09%)	
occurrences (all)	22	1	
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	2 / 14 (14.29%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Rash generalised			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Glycosuria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Urinary retention			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Bone pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	2 / 14 (14.29%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	3 / 14 (21.43%)	2 / 11 (18.18%)	
occurrences (all)	4	2	
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Infections and infestations			
Abscess oral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Device related infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Enterocolitis infectious			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Genital infection fungal			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Laryngitis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 14 (14.29%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Diabetes mellitus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Hyperglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hyperuricaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	2	1	

Hypomagnesaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Hypophosphataemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2014	- Clarification that the maximum treatment period is up to 2 years (a maximum of 26 Cycles). - Stage 0 gastric cancer added as a permitted prior and concurrent cancer. - An inclusion criterion was modified with respect to previous treatments / treatment duration total length of chemotherapy allowed was extended from 6 to 9 months. - Subjects who present with initial Stage I or II disease and then develop liver metastases and fulfill all of the other eligibility criteria were allowed to be enrolled.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
05 March 2015	Early termination of enrollment due to slow enrollment.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Decimal places were automatically truncated if last decimal equals zero.
This study was prematurely terminated. Analysis was not perfomed for primary and secondary outcome measures.

Notes: